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THE PHOTOCYCLOADDITION OF ISOCARBOSTYRIL TO OLEFINS

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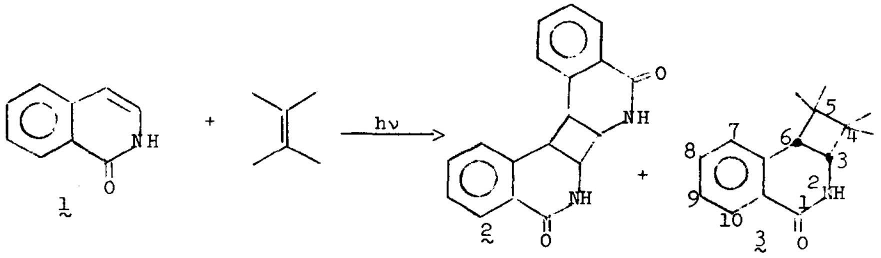
Recently we reported[1a] that the photochemical cycloaddition of carbostyrils to olefins formed 1:1 adducts in a regiospecific manner (only head-to-tail adducts were obtained). We would now like to describe some photocycloadditions of isocarbostyril to olefins to give 1:1 adducts. Isobutylene, tetramethylethylene and cyclopentene react with 1 in a manner similar to carbostyril. However, 1,1-dichloroethylene gives a mixture of head-to-tail and head-to-head isomers with isocarbostyril, but only the head-to-tail isomer with carbostyril. Furthermore, isocarbostyril reacts much less efficiently than carbostyril in both dimerization and cycloaddition reactions with olefins in the presence and absence of the sensitizers investigated.

A 700 ml ethanol solution of isocarbostyril (1, 7.25 g, 0.050 M) and tetramethylethylene (42 g, 0.50 M) was purged with N_2 and then irradiated for 9 days in a quartz vessel in a Rayonet Photochemical reactor equipped with 3500 Å Hg vapor black light fluorescent lamps. The products[2] obtained were .62 g (8.6%) 2 and 10.3 g (90%) 3; for 2:[3] mp 301-2° (from HOAc:EtOH:H_2O in 10:5:1); ir (KBr) 1653 cm^{-1} (amide C=O); nmr (CF_3CO_2D) δ 8.32 (m, 2, ArH), 7.67 (m, 6, ArH), 4.58 ppm (q, 4, -CH-CH-, J_{AB} = 8.5 Hz); for 3: mp 212.5-213.5° (from acetone, 76% overall yield); ir (KBr) 1663 cm^{-1} (amide C=O); uv λ_{max}^{EtOH} 230 mμ (ε 9550); nmr ($CDCl_3$) 8.17 (m, 1, ArH), 7.40 (m, 2, ArH), 7.05 (m, 1, ArH), 3.93, 3.57 (q, 2, -CH-CH-), $J_{3,6}$ = 9.0 Hz, $J_{3,2}$ = 2.5 Hz, 1.19, 1.17, 1.00, 0.78 ppm (4 s, 12, 4 CH_3).



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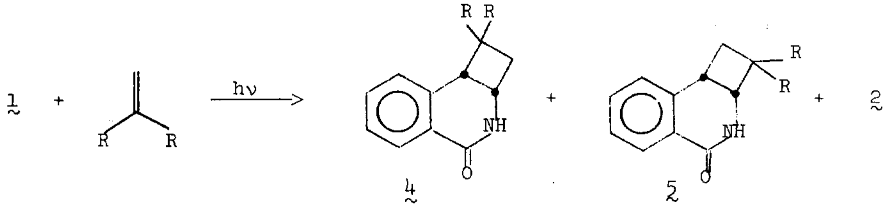
In the quartet centered at 3.74 δ, the downfield hydrogen on C-3 (3.90 δ) is coupled to the hydrogen on nitrogen (J = 2.5 Hz) and can be collapsed to a doublet by deuterium exchange with CD_3CO_2D. Because of the large coupling constant between H-6 and H-3 (9.0 Hz) and by analogy to the coumarin and carbostyril systems,[1] we have assigned the *cis*-configuration to the fused rings.

Photocycloaddition to 1,1-disubstituted olefins could have given a mixture of head-to-head and head-to-tail isomers.[4] In the reaction of **1** with isobutylene, however, only one isomer **4a** was obtained.



a, R=CH_3
b, R=Cl

A 700 ml N,N-dimethylacetamide solution of 6.00 g (.041 M) **1** and 31 g (.55 M) isobutylene gave after 6 days irradiation 1.8 g (30%) **2** and 5.8 g (70%) **4a**; shrinks 144-7°, turns pink and melts 147-159° (from acetone, 46%); ir (KBr) 1660 cm^{-1} (C=O); nmr ($CDCl_3$) δ 8.20 (*m*, 1, NH), 7.40 (*m*, 3, ArH), 7.04 (*m*, 1, ArH), 4.46 (*m*, 1, -CH-CH-NH, $J_{3,4\text{-}exo}$ = 6.8 Hz, $J_{3,4\text{-}endo}$ = 4.1 Hz, $J_{3,2}$ = 2.4 Hz), 3.53 (*d*, 1, -CH-CH-NH, $J_{3,6}$ = 9.1 Hz), 2.08 (*m*, 2, $-CH_2-$, $J_{4\text{-}exo,4\text{-}endo}$ = -11.4 Hz), 1.31, 0.85 ppm (2 *s*, 6, 2 CH_3). The hydrogens are readily assigned in this simple first order pattern by identifying the proton interacting with the hydrogen on nitrogen after deuterium exchange with CD_3CO_2D. The resulting simple first order ABKX pattern strongly supports the assigned structure for **4**. H-6 is a broad doublet at 3.53 δ, coupled by H-3 by 9.1 Hz; H-3, H-4 *exo* and H-4 *endo* are part of 12 line ABX pattern with H-3 at 4.46 δ as the X proton. The downfield proton (2.18 δ) of the AB pattern is assigned to H-4 *exo* because of the larger coupling to H-3 ($J_{3,4\ exo}$ = 6.8 Hz) than for the upfield proton at 1.98 δ (H-4 *endo*, $J_{3,4\text{-}endo}$ = 4.1 Hz), and because of the cross-ring long-range coupling with H-6 ($^4J_{6,4\text{-}exo}$ = 1.3 Hz).[5]

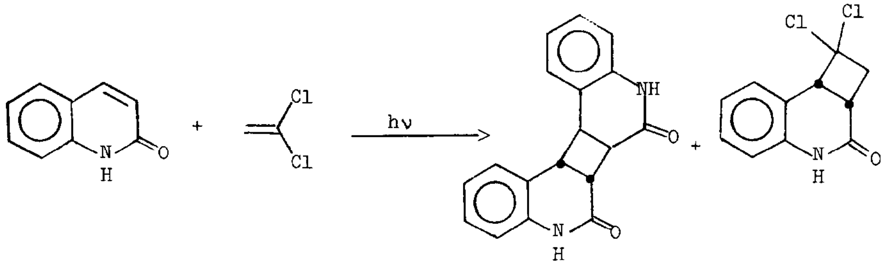
On the other hand, when isocarbostyril was irradiated with 1,1-dichloroethylene, a mixture of isomers **4b** and **5b** was obtained.

A 700 ml N,N-dimethylacetamide solution of 7.25 g (0.050 M) **1** and 48.5 g (0.50 M) 1,1-dichloroethylene gave after 5 days irradiation followed by column chromatography 10.0 g

(81%) **4b** and 2.23 g (19%) **5b**; for **4b**: mp 175.5-177.2° (from acetone, 57%); ir (KBr) 1665 cm^{-1} (C=O); λ_{max}^{MeOH} 228 mμ (ε 9680); R_f (tlc in 10% i-PrOH/ϕH-v/v) = 0.44; nmr (C_6D_6) δ 8.54 (*d*, 1, n-H); 7.05 (*m*, 2, ArH); 6.89 (*m*, 2, ArH); 3.86 (b*d*, 1, -CH-CH-N, $J_{6,3}$ = 9.0 Hz, $J_{6,4\text{-}exo}$ = 2.0 Hz); 3.62 (*m*, 1, -CH-C*H*-N, $J_{3,4\text{-}exo}$ = 6.5 Hz, $J_{3,4\text{-}endo}$ = 4.5 Hz, $J_{3,2}$ = 2.5 Hz); 2.67 (*m*, 1, H-4 *exo*, $J_{4\text{-}exo,\ 4\text{-}endo}$ = 13.5 Hz); and 2.54 ppm (*m*, 1, H-4 *endo*); for **5b**: mp 168-169°C (from acetone, 9.2%); ir (KBr) 1675 cm^{-1} (C=O); λ_{max}^{MeOH} 232mμ (ε 8430); R_f (tlc in 10% i-PrOH/ϕH-v/v) = .57; nmr ($CDCl_3$)[6] δ 8.18(*d*,1, N*H*), 7.32 (*m*, 4, Ar*H*) δ 4.78 (*m*, 1, -CH-C*H*-N, $J_{3,6}$ = 9.5 Hz, $J_{3,2}$ = 4.0 Hz, $J_{3,5\text{-}exo}$ = 2.0 Hz, $J_{3,5\text{-}endo}$ = 1.0 Hz); 4.06 (*t*/*d*, -C*H*-CH-N, $J_{6,5\text{-}exo}$ = 9.0 Hz, $J_{6,5\text{-}endo}$ = 5.5 Hz); 3.45 δ (d/d H-5 *exo*, $J_{5\text{-}exo,\ 5\text{-}endo}$ = 13.5 Hz); 3.03 ppm (*d*/*d*, H-5 *endo*).

The uv spectra of these isomers and other isocarbostyril photo-adducts are similar to that of benzamides.[7] The nmr spectra (220 MHz) are also consistent with the assigned structures; first order spectra were obtained in either C_6D_6 or $CDCl_3$ and all protons and coupling constants are readily assignable in these solvents.

In contrast to the observed behavior of isocarbostyril, irradiation of carbostyril (**6**) with 1,1-dichloroethylene gave only one adduct in addition to the dimer **7**.



6 **7** **8**

A 700 ml N,N-dimethylacetamide solution of 7.25 g (.05 M) **6** and 48.5 g (.50 M) 1,1-dichloroethylene gave in 3 days 2.2 g (30%) **7** and 8.39 g (70%) **8**; mp 198-199.5° (acetone, 72%); ir (KBr) 1670 cm^{-1} (C=O). The 220 MHz nmr (C_6D_6) of **8** presents a first-order pattern for the cyclobutane hydrogens which concurs with the assigned structure: H-6 is a doublet at 3.77 δ, broadened by cross-ring coupling, and coupled to H-3 by 10.0 Hz; H-3 appears as a triplet of doublets at 2.76 δ, with coupling to the geminal pair by 10.0 Hz and 3.5 Hz; H-4 *exo* is a doublet of doublets at 2.94 δ, assigned to the *exo* position due to the large $J_{3,4\text{-}exo}$ = 10.0 Hz, and has long-range cross-ring coupling to H-6 of 0.5 Hz; H-4 *endo* is a doublet of doublets at 3.17 δ assigned the *endo* position due to $J_{3,4\text{-}\underline{endo}}$ = 3.5 Hz and coupled to H-6 by $^{4}J_{6,4\text{-}\underline{endo}}$ = 1.5 Hz ($J_{4\text{-}\underline{exo},4\text{-}\underline{endo}}$ = 13.0 Hz).

Based on the above data, one could easily assign the head-to-head structure, analogous to **5**. However, there are two points that support our assignment: the chemical shift of the protons (H-6, H-4 *exo* and H-4 *endo*) adjacent to the geminal chlorines are shifted downfield and H-3 is shifted upfield from normal values (compare the carbostyril-isobutylene adduct[1a] and the isocarbostyril adducts) and carbostyril undergoes only head-to-tail addition to other 1,1-disubstituted olefins without formation of any isomer.

The presence of the two isomers **4b** and **5b** in this isocarbostyril system has mechanistic implications as to the nature of the excited species and is the subject of further investigation.

References

(1) a) G. R. Evanega and D. L. Fabiny, *Tetrahedron Letters*, 2241 (1968).
G. R. Evanega and D. L. Fabiny, *J. Org. Chem.* **35**, 1757 (1970).
E. B. Whipple and G. R. Evanega, *Org. Mag. Res.* **2**, 1 (1970).
b) J. W. Hanifin and E. Cohen, *Tetrahedron Letters*, 5401 (1968).

(2) All compounds have the correct elemental analyses and the correct MW: the latter was determined by the parent ion in the mass spec.

(3) The dimer could also be prepared in 36% yield by irradiating a solution of 1 in ethanol for 18 days. The stereochemistry of the dimer will be described in a later publication. The structure of the dimer is unknown. An analysis of the quartet nmr pattern by Dr. Earl B. Whipple (Union Carbide Research Institute) supports four possible structures: head-to-tail, *trans*-*transoid*-*trans*; head-to-tail, *trans*-*cisoid*-*trans*; head-to-tail, *cis*-*transoid*-*cis*; head-to-head, *cis*-*transoid*-*cis*. By anaology to data on related dimers published by L. Paolillo, H. Ziffer, and O. Buchardt, *J. Org. Chem.*, 35, 38 (1970), we favor the head-to-head, *cis*-*transoid*-*cis* structure.

(4) E. J. Corey, J. D. Bass, R. Le Mahieu and R. B. Mitra, *J. Am. Chem. Soc.*, **86**, 5570 (1964); B. D. Challand and P. de Mayo, *Chem. Commun*., 982 (1968)

(5) I. Fleming and D. H. Williams, *Tetrahedron*, 23, 2747 (1967).

(6) The nmr spectra are not directly comparable since different solvents were needed to resolve the complex 5 proton splitting pattern. Nevertheless, the analyses are self-consistent and support the proposed structures.

(7) Grols and Fisher, *Helv. Chim. Acta*, **38**, 1974 (1955).